RESPONSE

A. Status of the Claims

Claims 23-52 were pending at the time of the Office Action. Claim 23 has been amended to include subject matter from claim 26. Claim 26 has been canceled. Thus, claims 23-25 and 27-52 are now pending.

B. Objections to the Specification

The specification was objected to for containing embedded hyperlinks. Paragraphs [0112] and [0213] (as numbered in US 2006/0236432) have been amended to delete the embedded hyperlinks. Applicant, therefore, requests the withdrawal of this objection.

C. Objections to the Claims

The Action also objects to the claims for containing non-elected subject matter. Applicant traverses this rejection because the restriction requirement is improper.

The PCT Rules and the unity of invention standard apply to the present case. Under these standards, all of the content of the present claims relate to a single general inventive concept as required by PCT Rule 13.1, because they all contain the same or corresponding special technical features as required by PCT Rule 13.2. In this case, all of the claims and all of the claimed sequences relate to isolated nucleic acid molecule encoding a wild-type, nucleus-derived moss expression promoting region (MEPR).

The initial Restriction Requirement completely failed to meet the Office's burden of establishing why restriction between the claims is proper under the PCT Rules. The present Action appears to allege that the current claims do not possess a common special technical feature that defines a contribution over the Henschel and Komano references. However, as discussed below in regard to the art rejections, the currently claimed isolated nucleic acid molecule encoding a wild-type, nucleus-derived moss expression promoting region (MEPR) is

not disclosed by Henschel and/or Komano. Accordingly, there remains no evidence of record to dispute that there is a common inventive feature among the claims. In view of the above, the "inventions" set forth in the Restriction Requirement have a common inventive concept as required by PCT Rule 13.2, and Applicant requests withdrawal of the Restriction Requirement and examination of all pending claims in the present case.

Additionally, the Action's apparent position that it is appropriate to examine only a single nucleic acid sequence in an application is inconsistent with Director's decision to permit a reasonable number of nucleic acid sequences to be claimed in a single application. MPEP § 803.04 (citing *Examination of Patent Applications Containing Nucleotide Sequences*, 1192 O.G. 68 (November 19, 1996)). In this regard, the MPEP further advises that "normally ten sequences constitute a reasonable number for examination purposes. Accordingly, in most cases, up to ten independent and distinct nucleotide sequences will be examined in a single application without restriction. In addition to the specifically selected sequences, those sequences which are patentably indistinct from the selected sequences will also be examined." MPEP § 803.04.

In traversing the restriction requirement on the grounds set forth above, Applicant takes no position with regard to whether any sets of the present claims or any individual present claims are or are not patentably distinct from any other set of claims or individual claim. Rather, Applicant argues without acquiescence that, under the circumstances of this case and in view of the applicable PCT rules and statements of the MPEP, the stated restriction is not proper, whether those claims are patentably distinct or not. Such arguments do not create an estoppel against Applicant and are not an admission that the restricted Groups are either patentably distinct or patentably indistinct from one another.

In view of the above, Applicant requests withdrawal of the Restriction Requirement and examination of the full scope of the pending claims in the present case.

D. The Claims Are Enabled

Claims 23-52 are rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Action acknowledges that the specification is enabling for SEQ ID NO: 13, but asserts that the specification is not enabling for all nucleus-derived expression promoting regions from all mosses. The Action alleges that the skilled artisan could not make and use the claimed invention without undue experimentation because no other sequences have been demonstrated to function as a promoter, that the promoter sequence was only shown to work in one moss species, and that the function of promoter fragments and variants is unpredictable. Applicant traverses this rejection.

The current claims are enabled because a person of ordinary skill in the art could make and use the claimed invention without under experimentation. Current claim 23 is directed to an isolated nucleic acid molecule comprising a wild-type, nucleus-derived moss expression promoting region (MEPR) comprising any of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 20, 24, 25, or 26 or an expression promoting fragment of any of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 20, 24, 25, or 26. A person of ordinary skill in the art could make a nucleic acid molecule comprising SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 20, 24, 25, or 26 without undue experimentation because these sequences are expressly disclosed in the specification. One could also use a nucleic acid molecule comprising SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 20, 24, 25, or 26 without undue experimentation because the specification demonstrates that these are MEPRs having an expression promoting activity that is at least equal to the expression promoting activity of CaMV 35 S promoter, which is the "gold standard" promoter in plant technology (*see e.g.,* Specification, FIGs. 2-6, 8-17, and related text).

One of ordinary skill in the art could also make and use an expression promoting fragment of any of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 20, 24, 25, or 26. As defined in the

specification, an "expression promoting fragment" of an MPER is a fragment that has an expression promoting activity of at least 30%, preferably at least 50%, of the expression promoting activity of a working heterologous promoter (e.g., CaMV 35S) in the specific host cell (Specification, para. [0017]). As noted above, the specification discloses the sequences of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 20, 24, 25, or 26 and demonstrates that these sequences, as well as various fragments of these sequences, have expression promoting activity. In addition, Examples 1 and 2 in the specification disclose methods with which a person of ordinary skill in the art can screen fragments of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 20, 24, 25, or 26 for expression promoting activity. In light of the guidance in the specification, such routine screening would not constitute undue experimentation. *See e.g., In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

Finally, the articles of Kim et al., Donald et al. and Dolferus et al. cited on page 4 of the present Action do not provide evidence of a lack of enablement because they do not relate to MEPRs. Furthermore, these articles are representative for a state of the art 10 years or more before the filing date of the present application. In contrast to the old technology described in these articles, the present specification contains a modern assay system for clearly defining the functionality of the promoting activity of MEPRs, and defines the functionality of the MEPRs relative to the functionality to the best known and most frequently used promoter model in plants, namely the CaMV 35 S promoter, which cannot be regarded as unknown or unpredictable at the time the present application was filed.

In view of the above, the present specification contains a description sufficient to enable one skilled in the art to make and use the claimed invention without unduly extensive experimentation. The claims, therefore, are enabled and the rejection should be withdrawn.

E. The Claims Are Supported by Adequate Written Description

Claims 23-52 are rejected under 35 U.S.C. § 112, first paragraph, for lack of written description. In particular, the Action alleges that the claims encompass millions of isolated sequences from multiple species of moss, but the specification only describes SEQ ID NOs.: 1-27 as moss expression promoting regions. Thus, the Action asserts that the specification does not adequately describe the claimed expression promoting regions through the description of a representative number of species or through an identification of the structures responsible for the expression promoting function of these sequences. Applicant traverses this rejection.

The current claims are supported by adequate written description because a person of ordinary skill in the art would recognize that the inventors were in possession of the claimed subject matter at the time of filing. Current claim 23 is directed to an isolated nucleic acid molecule comprising a wild-type, nucleus-derived moss expression promoting region (MEPR) comprising any of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 20, 24, 25, or 26 or an expression promoting fragment of any of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 20, 24, 25, or 26. Clearly the inventors were in possession of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 20, 24, 25, and 26. It would also be evident to one of ordinary skill in the art that the inventors were in possession of expression promoting fragments of any of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 20, 24, 25, and 26. "Expression promoting fragments" of an MPER are fragments that have an expression promoting activity of at least 30%, preferably at least 50%, of the expression promoting activity of a working heterologous promoter (e.g., CaMV 35S) in the specific host cell (Specification, para. [0017]). The specification also demonstrates that various fragments of the claimed sequences have expression promoting activity (*see e.g.,* Specification, FIGs. 2-6, 8-17, and related text).

The Action's reliance on *Eli Lilly* and *Amgen* is not applicable to the current claims. *Eli Lilly* requires only that claims to genetic material require recitation of more than a mere function. *Eli Lilly*, 119 F.3d 1559, 1568 ("In claims to genetic material, however, a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function."). As discussed above, the current claims of the present application recite more than a mere function. Moreover, while the current claims are supported by a recitation of structure (*i.e.,* DNA sequence), Applicant notes that the Federal Circuit's more recent opinion in *Falkner v. Inglis* clarified that "there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure." *Falkner v. Inglis*, 448 F.3d 1357, 1366 (Fed. Cir. 2006).

In view of the above, the present specification describes the claimed invention in sufficient detail that one of ordinary skill in the art can reasonably conclude that Applicant had possession of the claimed invention at the time of filing. Applicant, therefore, requests the withdrawal of this rejection.

F. The Claims Are Definite

Claims 23-52 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. In particular, the Action states that it is unclear how an expression promoting region is "encoded" because this term typically refers to sequences that "encode" proteins. This rejection is moot in view of the amendment to claim 23 that replaces the term "encoding" with "comprising."

G. The Claims Are Novel Over Henschel et al.

Claims 23-28 and 34-35 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Henschel *et al.* (Mol. Biol. Evol. 19:801-814 (2002)). Applicant traverses this rejection.

The Action's initial assertions (Action, p. 8) that (1) the claims are broadly drawn to any isolated nucleic acid that encodes a wild-type nucleus-derived moss expression promoting region, and (2) the phrase "a" sequence of SEQ ID NO: 13 reads on any 2 bp of SEQ ID NO: 13, are moot in view of the current claims. Current claim 23 recites "An isolated nucleic acid molecule... comprising any of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 20, 24, 25, or 26 or an expression promoting fragment of any of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 20, 24, 25, or 26." Thus, current claim 20 is not directed to "any" isolated MEPR, but only to those comprising the recited SEQ ID NOs or fragments thereof. In addition, any fragments of the recited SEQ ID NOs are "expression promoting fragment[s]." Accordingly, current claim 23 does not read on "any" 2 bp fragment of the recited SEQ ID NOs as asserted in the Action.

Turning now to the Henschel reference, the Action states that Henschel teaches the isolation of genes from *Physcomitrella patens*, including promoter regions, which are cloned into bluescript. The Action does not identify any promoter in Henschel comprising any of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 20, 24, 25, or 26 or an expression promoting fragment of any of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 20, 24, 25, or 26. Rather, the Action appears to rely on the argument that a promoter sequence comprising any 2 bp fragment of the claimed SEQ ID NOs anticipates the claims. As discussed above, however, such a reading of the current claims is incorrect. The Action fails to establish a *prima facie* case of anticipation against the current claims because the Action does not identify any promoter in Henschel comprising any of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 20, 24, 25, or 26 or an expression promoting fragment of any of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 20, 24, 25, or 26. For at least this reason the present rejection should be withdrawn.

In addition to not disclosing nucleic acid molecules comprising the specific sequences recited in current claim 23, Henschel also fails to teach a wild-type, nucleus-derived moss

expression promoting region (MEPR) generally. Henschel characterized putative MADS-box genes. The characterization was based on the cloning of cDNA and genomic gene regions and the comparison of these sequences with sequences and structures of known MADS-box genes by sequence comparison. The cloning of the putative Physcomitrella gene exclusively served these *in silico* comparisons of intron-exon structures and was not for functional verification of the genes (see Henschel et al., page 812, second column, second paragraph: "The functions of the genes reported here still have to be determined"). In fact, in this article not even a Northern blot is described which at least would have at least provided evidence of the expression of the putative genes on transcript level. The lack of expression data inevitably shows that the surrounding 5', 3', and genomic sequences at best could have "putative" promoter character. This was explicitly conceded by the authors (see page 804, first column, second paragraph: "Sequence information of putative promoter regions and 5' untranslated regions..."; and page 812, first column, third paragraph: "An analysis of the putative promoter region of PPM2...").

Cloning of putative promoter regions was only vaguely described in the materials and methods section on page 804, first column, second paragraph. The method per se (RAGE) is mentioned; primers for the amplification of putative promoter elements are, however, not specified (see page 804, first column, fourth paragraph). Only for PPM4 it was noted that primers of the cloned cDNA sequence were used. For other putative promoter regions, not even the cloning is described. Thus, Henschel does not provide a repeatable or enabling disclosure of a functional moss promoter.

In view of the above, the current claims are novel over Henschel. Applicant, therefore, requests the withdrawal of this rejection.

H. The Claims Are Patentable Over Henschel et al. and Komano et al.

The Action rejects claims 23-28 and 33-52 under 35 U.S.C. § 103(a) as being obvious over Henschel in view of Komano *et al.* (U.S. Patent 4,710,461). Applicant traverses this rejection.

As was the case with the anticipation rejection, the Action's initial assertions (Action, p. 9) in regard to the obviousness rejection that (1) the claims are broadly drawn to any isolated nucleic acid that encodes a wild-type nucleus-derived moss expression promoting region, and (2) the phrase "a" sequence of SEQ ID NO: 13 reads on any 2 bp of SEQ ID NO: 13, are moot in view of the current claims. The Action does not identify any sequence in Henschel or Komano comprising any of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 20, 24, 25, or 26 or an expression promoting fragment of any of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 20, 24, 25, or 26 as recited in current claim 23. Accordingly, the Action fails to establish a *prima facie* case of obviousness because the alleged combination of Henschel and Komano would not result in the nucleic acid molecule recited in current claim 23. For at least this reason the present obviousness rejection should be withdrawn.

Additionally, Komano described the isolation and use of a ***chloroplast*** (*i.e.,* not ***nucleus-derived***) promoter in ***prokaryotes***. The example described by Komano (expression of β-galactosidase under the chloroplast promoter in *E. coli*) cannot be successfully carried out with nucleus-derived promoters, which do not function in *E. coli*. Accordingly, one of ordinary skill in the art would not have had an apparent reason to replace the chloroplast promoter with a nucleus-derived promoter to express recombinant polypeptides in *E. coli* as described by Komano. Thus, this is additional evidence that the current claims are not obvious in view of Henschel and Komano.

In view of the above, the current claims are patentable over Henschel and Komano. Applicant, therefore, requests the withdrawal of this rejection.

I. Conclusion

Applicant believes this paper to be a full and complete response to the Office Action dated October 5, 2008. Applicant respectfully request favorable consideration of this case in view of the above comments and amendments. Should the Examiner have any questions, comments, or suggestions relating to this case, the Examiner is invited to contact the undersigned Applicants' representative at (512) 536-5654.

Respectfully submitted,

Travis M. Wohlers
Reg. No. 57,423
Attorney for Applicant

CUSTOMER NO. 32425
FULBRIGHT & JAWORSKI L.L.P.
600 Congress Avenue, Suite 2400
Austin, Texas 78701
512.536.5654 (voice)
512.536.4598 (fax)

Date: April 7, 2008